**Supplementary material to**

**Prenatal depressive symptoms, DNA methylation of HPA related genes and basal cortisol in children**

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## Table S1. *Child diurnal cortisol measures: descriptive statistics and mean sampling time of valid samples*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Total | | Prenatal depressive symptomsa | | | | | Non-exposed vs. exposed | | |
|  | Non-exposed | | | Exposed | |
|  | *n* | Mean (*SD*) | *n* | Mean (*SD*) | *n* | | Mean (*SD*) | *t*(79-144) | *p* | *d* |
| Cortisol levels (nmol/l) | | | | | | | | | |  |
| T1 | 99 | 17.86 (9.06) | 68 | 17.62 (9.22) | 31 | | 18.38 (8.82) | 0.39 | .700 | 0.09 |
| T2 | 119 | 18.78 (8.46) | 82 | 17.75 (7.62) | 37 | | 21.06 (9.82) | 2.00\* | .047 | 0.40 |
| T3 | 144 | 5.58 (2.35) | 100 | 5.45 (2.36) | 44 | | 5.89 (2.32) | 1.04 | .302 | 0.19 |
| T4 | 145 | 3.81 (1.66) | 101 | 3.82 (1.71) | 44 | | 3.80 (1.57) | 0.07 | .942 | 0.01 |
| T5 | 146 | 1.86 (1.04) | 102 | 1.90 (0.98) | 44 | | 1.76 (1.17) | 0.73 | .467 | 0.13 |
| Sampling time information | | | | | | | | | |  |
| Awakening time | 133 | 07:30 (0:59) | 91 | 07:18 (0:54) | 42 | | 07:55 (1:02) | 3.49\*\* | .001 | 0.65 |
| Time T1 | 99 | 07:40 (1:00) | 68 | 07:28 (0:55) | 31 | | 08:06 (1:04) | 2.97\*\* | .004 | 0.64 |
| Time T2 | 119 | 08:16 (1:00) | 82 | 08:03 (0:55) | 37 | | 08:46 (1:01) | 3.76\*\* | <.001 | 0.75 |
| Time T3 | 144 | 12:36 (1:06) | 100 | 12:34 (1:07) | 44 | | 12:40 (1:02) | 0.55 | .587 | 0.10 |
| Time T4 | 145 | 17:21 (0:44) | 101 | 17:22 (0:45) | 44 | | 17:19 (0:40) | 0.36 | .716 | 0.07 |
| Time T5 | 146 | 20:26 (1:00) | 102 | 20:26 (1:03) | 44 | | 20:27 (0:55) | 0.10 | .918 | 0.02 |
| Awakening – T1 (min) | 99 | 6.67 (5.12) | 68 | 6.26 (5.32) | 31 | | 7.55 (4.62) | 1.16 | .250 | 0.25 |
| T1 – T5 (hours) | 145 | 12.75 (1.34) | 101 | 12.93 (1.33) | 44 | | 12.32 (1.31) | 2.55\* | .012 | 0.46 |

(continued)

**Table S1** (continued)

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Total | | Prenatal depressive symptoms (EPDS)a | | | | | Non-exposed vs. exposed | | |
|  | Non-exposed | | | Exposed | |
|  | *n* | Mean (*SD*) | *n* | Mean (*SD*) | | *n* | Mean (*SD*) | *t*(79-144) | *p* | *d* |
| Diurnal cortisol parametersb | | | | | | | | | |  |
| Waking Cortisol | 99 | 2.81 (0.56) | 68 | | 2.79 (0.58) | 31 | 2.85 (0.51) | 0.54 | .589 | 0.12 |
| Bedtime Cortisol | 145 | 0.99 (0.33) | 101 | | 1.00 (0.31) | 44 | 0.95 (0.37) | 1.00 | .318 | 0.18 |
| CAR | 81 | 0.05 (0.17) | 56 | | 0.03 (0.18) | 25 | 0.08 (0.16) | 1.11 | .269 | 0.27 |
| Diurnal Slope | 99 | -0.13 (0.05) | 68 | | -0.13 (0.05) | 31 | -0.14 (0.05) | 1.44 | .154 | 0.31 |
| Total release | 145 | 23.40 (3.96) | 101 | | 23.62 (3.95) | 44 | 22.91 (3.97) | 1.00 | .319 | 0.18 |

*Note:* Default sampling times: T1 = at awakening. T2 = 30 minutes after awakening. T3 = 12 a.m.. T4 = 5 p.m.. T5 at bedtime. Exclusion of participants due to diseases. medication or technical problems. Exclusion of T1 samples with >15 minutes since awakening from analyses of waking cortisol, CAR and diurnal slope analyses. Exclusion of T2 samples with <15 Minutes or >45 minutes since awakening from CAR analyses. CAR = Cortisol awakening response. Total release = total cortisol release throughout the day. *t*-statisticsand *p*-values refer to the independent t-test, with *t*-scores displayed as absolute values. Cohen’s *d* indicate effect size: *d* = 0.2-0.5 small effect, *d* = 0.5-0.8 medium effect, *d* > 0.8 large effect (Cohen, 1988). aPrenatal EPDS (Edinburgh Postnatal Depression Scale; Cox, Holden, & Sagovsky, 1987) score < 10 interpreted as non-exposed, ≥ 10 as exposed. bbased on ln-transformed raw cortisol values. \**p* < .05. \*\**p* < .01.

## Table S2. *Correlations between child cortisol parameters and potential covariates*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Waking Cortisol  (*n* = 99) | Bedtime Cortisol  (*n* = 145) | CAR  (*n* = 81) | Diurnal Slope  (*n* = 99) | Total release  (*n* = 145) |
| SES | .138 | -.018 | .056 | -.127 | .118 |
| Agea | .136 | .007 | -.005 | -.175 | .051 |
| Sex | .007 | -.034 | -.060 | -.027 | -.022 |
| Emotional problems (SDQ) | .068 | .050 | -.171 | -.045 | -.087 |
| Conduct problems (SDQ) | .158 | .100 | -.068 | -.020 | .022 |
| Gestational age | .360 | .825 | .793 | .231 | .766 |
| Birth weight | .398 | .306 | .291 | .483 | .079 |
| Apgar | .169 | -.206\* | -.036 | -.276\*\* | -.045 |
| Alcohol consumption pre | -.012 | -.038 | -.152 | -.082 | -.047 |
| Cigarette smoking pre | -.065 | -.012 | .038 | .035 | -.100 |
| Antibiotica intake | .216\* | -.079 | -.040 | -.169 | .042 |
| School day | -.144 | .081 | -.044 | .137 | -.341\*\* |
| Time Awakening - T1 | .006 | .095 | .105 | -.023 | -.220\*\* |
| Time T1 - T5 | -.028 | -.235\*\* | .252\* | .119 | .641\*\* |
| EPDS post | .017 | .034 | -.019 | .012 | -.001 |
| EPDS current | -.058 | .108 | .001 | .078 | .074 |

*Note*: Correlations are Pearson product-moment-correlation coefficients. CAR = cortisol awakening response. Total release = total cortisol release throughout the day. SES = socioeconomic family status. SDQ = Strength and Difficulties Questionnaire (Goodman, 2001). EPDS = Edinburgh Postnatal Depression Scale (Cox et al., 1987). Pre = prenatal, post = postnatal. aat time of cortisol and DNA sampling. \**p* < .05. \*\* *p* < .01.

## Table S3. *Sex-specific effects of exposure to prenatal depressive symptoms on diurnal cortisol parameters and DNA methylation: results of post-hoc ANCOVAs, separately for the non-exposed and exposed group*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Diurnal Cortisol Parameters | | | Boys vs. girls | | | | | |
|  | |  | Non-exposeda  *(n* = 101) | | | Exposeda  *(n* = 44) | | |
|  | |  | *F* | *p* | ηp2 | *F* | *p* | ηp2 |
| Bedtime Cortisolb.c | | | 1.56 | .215 | .02 | 2.80 | .103 | .07 |
| Total releaseb.d | | | 2.97 | .088+ | .03 | 3.28 | .078+ | .08 |
| DNA methylation | | | Boys vs. girls | | | | | |
|  | | | Non-exposeda  *(n* = 117) | | | Exposeda  *(n* = 50) | | |
| Gene | CpG | | *F* | *p* | ηp2 | *F* | *p* | ηp2 |
| *NR3C1* | cg04111177 | | 1.60 | .208 | .01 | 3.54 | .066+ | .07 |
| *NR3C1* | cg27107893 | | 1.10 | .297 | .01 | 3.25 | .080+ | .09 |
| *SLC6A4* | cg26741280 | | 1.09 | .298 | .01 | 3.06 | .087+ | .06 |

*Note*. Total release = total cortisol release throughout day. aPrenatal EPDS (Edinburgh Postnatal Depression Scale; Cox et al., 1987) score <10 interpreted as non-exposed, ≥10 as exposed. Models were adjusted for maternal postnatal and current depressive symptoms as well as specific covariates for the cortisol parameters: btime between first and last sample, cmean Apgar score, dschool day (yes/no). +*p* < .10

## Table S4*. Effects of exposure to prenatal depressive symptoms and sex on DNA methylation: results of ANCOVAs*

|  |  |  | ME EPDSpre | | | IA EPDSpre x sex | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Gene | CpG | Position | *F* | *p* | ηp2 | *F* | *p* | ηp2 |
| *BDNF* | cg01225698 | Chr11: 27742355 | 3.68 | .057 | .02 | 0.00 | .957 | .00 |
| *BDNF* | cg02527472 | Chr11: 27743348 | 0.87 | .352 | .01 | 1.05 | .308 | .01 |
| *BDNF* | cg02613510 | Chr11: 27723790 | 0.37 | .546 | .00 | 0.06 | .805 | .00 |
| *BDNF* | cg03167496 | Chr11: 27743619 | 3.30 | .071 | .02 | 0.06 | .811 | .00 |
| *BDNF* | cg03747251 | Chr11: 27722722 | 0.08 | .774 | .00 | 0.14 | .706 | .00 |
| *BDNF* | cg03984780 | Chr11: 27722617 | 0.04 | .839 | .00 | 0.68 | .411 | .00 |
| *BDNF* | cg04106006 | Chr11: 27742454 | 0.13 | .721 | .00 | 0.00 | .955 | .00 |
| *BDNF* | cg04481212 | Chr11: 27740495 | 0.27 | .606 | .00 | 2.45 | .120 | .02 |
| *BDNF* | cg04672351 | Chr11: 27722889 | 1.28 | .260 | .01 | 1.37 | .244 | .01 |
| *BDNF* | cg05218375 | Chr11: 27723218 | 0.20 | .652 | .00 | 2.57 | .111 | .02 |
| *BDNF* | cg06684850 | Chr11: 27742369 | 1.92 | .168 | .01 | 0.03 | .864 | .00 |
| *BDNF* | cg06816235 | Chr11: 27742219 | 0.33 | .565 | .00 | 0.00 | .983 | .00 |
| *BDNF* | cg07704699 | Chr11: 27742832 | 0.98 | .324 | .01 | 2.36 | .126 | .01 |
| *BDNF* | cg10022526 | Chr11: 27744557 | 3.39 | .067 | .02 | 0.08 | .780 | .00 |
| *BDNF* | cg10635145 | Chr11: 27742435 | 0.13 | .723 | .00 | 0.52 | .471 | .00 |
| *BDNF* | cg11718030 | Chr11: 27744363 | 0.39 | .535 | .00 | 1.11 | .294 | .01 |
| *BDNF* | cg11806762 | Chr11: 27732958 | 0.11 | .741 | .00 | 0.17 | .681 | .00 |
| *BDNF* | cg15462887 | Chr11: 27744049 | 1.16 | .283 | .01 | 0.01 | .925 | .00 |
| *BDNF* | cg17413943 | Chr11: 27739827 | 0.13 | .725 | .00 | 0.48 | .490 | .00 |
| *BDNF* | cg18595174 | Chr11: 27701991 | 0.41 | .523 | .00 | 0.62 | .431 | .00 |
| *BDNF* | cg20108357 | Chr11: 27718978 | 0.06 | .812 | .00 | 0.95 | .330 | .01 |
| *BDNF* | cg23497217 | Chr11: 27723214 | 0.01 | .944 | .00 | 0.16 | .693 | .00 |
| *BDNF* | cg23619332 | Chr11: 27722060 | 0.09 | .765 | .00 | 0.38 | .537 | .00 |
| *BDNF* | cg24065044 | Chr11: 27723409 | 0.04 | .835 | .00 | 0.51 | .477 | .00 |
| *BDNF* | cg24249411 | Chr11: 27744759 | 0.55 | .458 | .00 | 2.56 | .112 | .02 |
| *BDNF* | cg25457956 | Chr11: 27743664 | 0.08 | .782 | .00 | 0.21 | .649 | .00 |
| *BDNF* | cg25962210 | Chr11: 27721222 | 0.33 | .568 | .00 | 0.66 | .416 | .00 |
| *BDNF* | cg26840770 | Chr11: 27723290 | 0.21 | .651 | .00 | 0.06 | .802 | .00 |
| *BDNF* | cg26949694 | Chr11: 27742060 | 0.03 | .862 | .00 | 0.48 | .491 | .00 |
| *BDNF* | cg27351358 | Chr11: 27743258 | 0.10 | .756 | .00 | 0.85 | .359 | .01 |
| *BDNF* | cg09606766 | Chr11: 27722971 | 3.32 | .070 | .02 | 1.02 | .314 | .01 |
| *BDNF* | cg01583131 | Chr11: 27744675 | 0.00 | .969 | .00 | 0.11 | .738 | .00 |
| *BDNF* | cg06260077 | Chr11: 27721350 | 0.29 | .592 | .00 | 0.31 | .579 | .00 |
| *BDNF* | cg07159484 | Chr11: 27722523 | 0.09 | .769 | .00 | 3.44 | .065 | .02 |
| *BDNF* | cg11241206 | Chr11: 27723128 | 0.01 | .917 | .00 | 0.00 | .954 | .00 |

(continued)

**Table S6** (continued)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | ME EPDSpre | | | IA EPDSpre x sex | | |
| Gene | CpG | Position | *F* | *p* | ηp2 | *F* | *p* | ηp2 |
| *BDNF* | cg22043168 | Chr11: 27741077 | 1.44 | .233 | .01 | 0.27 | .602 | .00 |
| *BDNF* | cg24377657 | Chr11: 27723245 | 1.48 | .226 | .01 | 3.55 | .061 | .02 |
| *BDNF* | cg25412831 | Chr11: 27742138 | 1.54 | .216 | .01 | 0.09 | .770 | .00 |
| *BDNF* | cg27193031 | Chr11: 27721088 | 0.45 | .504 | .00 | 0.53 | .467 | .00 |
| *CRHR1* | cg00022871 | Chr17: 43884358 | 0.95 | .332 | .01 | 0.02 | .884 | .00 |
| *CRHR1* | cg00025823 | Chr17: 43909151 | 0.07 | .790 | .00 | 1.17 | .281 | .01 |
| *CRHR1* | cg07778819 | Chr17: 43862927 | 0.53 | .466 | .00 | 0.94 | .333 | .01 |
| *CRHR1* | cg08929103 | Chr17: 43860355 | 0.53 | .467 | .00 | 0.04 | .849 | .00 |
| *CRHR1* | cg16642545 | Chr17: 43878769 | 2.05 | .154 | .01 | 0.86 | .355 | .01 |
| *CRHR1* | cg16830379 | Chr17: 43912434 | 0.00 | .959 | .00 | 0.32 | .574 | .00 |
| *CRHR1* | cg18757974 | Chr17: 43860691 | 1.85 | .176 | .01 | 1.55 | .216 | .01 |
| *CRHR1* | cg24063856 | Chr17: 43863303 | 0.14 | .705 | .00 | 0.15 | .700 | .00 |
| *CRHR1* | cg24353392 | Chr17: 43862247 | 0.58 | .447 | .00 | 0.34 | .559 | .00 |
| *CRHR1* | cg24394631 | Chr17: 43863000 | 0.10 | .749 | .00 | 3.83 | .052 | .02 |
| *CRHR1* | cg27410679 | Chr17: 43866278 | 0.07 | .794 | .00 | 1.40 | .238 | .01 |
| *CRHR1* | cg27551605 | Chr17: 43862910 | 1.60 | .208 | .01 | 0.75 | .387 | .01 |
| *CRHR1* | cg27503360 | Chr17: 43890749 | 3.31 | .071 | .02 | 1.86 | .174 | .01 |
| *CRHR1* | cg04856689 | Chr17: 43862032 | 0.00 | .975 | .00 | 1.81 | .180 | .01 |
| *CRHR1* | cg26656751 | Chr17: 43910226 | 0.15 | .701 | .00 | 1.27 | .261 | .01 |
| *FKBP5* | cg00052684 | Chr6: 35694245 | 0.52 | .472 | .00 | 0.29 | .590 | .00 |
| *FKBP5* | cg00130530 | Chr6: 35657202 | 0.11 | .742 | .00 | 0.69 | .406 | .00 |
| *FKBP5* | cg00610228 | Chr6: 35695934 | 0.18 | .676 | .00 | 0.02 | .883 | .00 |
| *FKBP5* | cg01294490 | Chr6: 35656906 | 2.81 | .095 | .02 | 0.23 | .632 | .00 |
| *FKBP5* | cg02665568 | Chr6: 35544468 | 0.35 | .553 | .00 | 0.80 | .371 | .01 |
| *FKBP5* | cg03546163 | Chr6: 35654363 | 0.00 | .989 | .00 | 3.69 | .056 | .02 |
| *FKBP5* | cg03591753 | Chr6: 35659141 | 0.33 | .567 | .00 | 0.39 | .534 | .00 |
| *FKBP5* | cg06087101 | Chr6: 35551932 | 2.99 | .086 | .02 | 1.99 | .160 | .01 |
| *FKBP5* | cg07061368 | Chr6: 35631736 | 0.13 | .722 | .00 | 0.02 | .877 | .00 |
| *FKBP5* | cg07633853 | Chr6: 35569471 | 0.60 | .439 | .00 | 3.38 | .068 | .02 |
| *FKBP5* | cg08586216 | Chr6: 35612351 | 0.23 | .632 | .00 | 1.19 | .278 | .01 |
| *FKBP5* | cg08636224 | Chr6: 35657921 | 0.03 | .868 | .00 | 1.36 | .245 | .01 |
| *FKBP5* | cg08915438 | Chr6: 35697759 | 1.30 | .256 | .01 | 0.01 | .932 | .00 |
| *FKBP5* | cg10300814 | Chr6: 35565116 | 0.10 | .752 | .00 | 0.79 | .376 | .01 |
| *FKBP5* | cg14284211 | Chr6: 35570224 | 0.31 | .581 | .00 | 0.05 | .829 | .00 |
| *FKBP5* | cg14642437 | Chr6: 35652521 | 1.03 | .312 | .01 | 0.03 | .855 | .00 |
| *FKBP5* | cg16012111 | Chr6: 35656758 | 0.80 | .374 | .01 | 0.80 | .371 | .01 |

(continued)

**Table S6** (continued)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | ME EPDSpre | | | IA EPDSpre x sex | | |
| Gene | CpG | Position | *F* | *p* | ηp2 | *F* | *p* | ηp2 |
| *FKBP5* | cg16052510 | Chr6: 35603143 | 0.32 | .572 | .00 | 0.33 | .569 | .00 |
| *FKBP5* | cg17085721 | Chr6: 35645341 | 1.04 | .310 | .01 | 0.02 | .878 | .00 |
| *FKBP5* | cg19014730 | Chr6: 35635985 | 1.62 | .205 | .01 | 0.93 | .337 | .01 |
| *FKBP5* | cg19226017 | Chr6: 35697185 | 0.08 | .779 | .00 | 0.14 | .710 | .00 |
| *FKBP5* | cg20813374 | Chr6: 35657180 | 0.04 | .835 | .00 | 0.75 | .389 | .01 |
| *FKBP5* | cg25114611 | Chr6: 35696870 | 2.56 | .111 | .02 | 0.01 | .930 | .00 |
| *FKBP5* | cg00140191 | Chr6: 35656242 | 1.37 | .244 | .01 | 0.00 | .998 | .00 |
| *FKBP5* | cg15929276 | Chr6: 35687457 | 0.11 | .741 | .00 | 0.28 | .596 | .00 |
| *FKBP5* | cg18726036 | Chr6: 35543610 | 2.73 | .101 | .02 | 0.20 | .658 | .00 |
| *NR3C1* | cg03857453 | Chr5: 142729913 | 1.25 | .266 | .01 | 2.80 | .096 | .02 |
| *NR3C1* | cg04111177 | Chr5: 142783607 | 1.11 | .294 | .01 | 4.73\* | .031 | .03 |
| *NR3C1* | cg06613263 | Chr5: 142779552 | 1.28 | .259 | .01 | 0.06 | .804 | .00 |
| *NR3C1* | cg07528216 | Chr5: 142788776 | 0.50 | .480 | .00 | 0.10 | .749 | .00 |
| *NR3C1* | cg07733851 | Chr5: 142781498 | 4.68\* | .032 | .03 | 0.22 | .644 | .00 |
| *NR3C1* | cg08818984 | Chr5: 142814827 | 1.41 | .237 | .01 | 1.64 | .202 | .01 |
| *NR3C1* | cg08845721 | Chr5: 142780693 | 2.43 | .121 | .02 | 0.01 | .919 | .00 |
| *NR3C1* | cg12466613 | Chr5: 142815469 | 0.13 | .717 | .00 | 0.87 | .354 | .01 |
| *NR3C1* | cg13648501 | Chr5: 142785258 | 0.26 | .609 | .00 | 0.76 | .385 | .01 |
| *NR3C1* | cg16586394 | Chr5: 142757011 | 0.06 | .800 | .00 | 0.23 | .629 | .00 |
| *NR3C1* | cg18484679 | Chr5: 142740314 | 0.15 | .700 | .00 | 1.47 | .227 | .01 |
| *NR3C1* | cg18849621 | Chr5: 142784382 | 0.13 | .719 | .00 | 0.11 | .741 | .00 |
| *NR3C1* | cg19457823 | Chr5: 142692961 | 1.69 | .196 | .01 | 0.02 | .877 | .00 |
| *NR3C1* | cg23273257 | Chr5: 142658828 | 0.07 | .796 | .00 | 1.17 | .282 | .01 |
| *NR3C1* | cg25535999 | Chr5: 142757312 | 2.07 | .152 | .01 | 2.97 | .087 | .02 |
| *NR3C1* | cg26720913 | Chr5: 142814934 | 0.06 | .805 | .00 | 0.02 | .891 | .00 |
| *NR3C1* | cg27107893 | Chr5: 142776274 | 0.12 | .731 | .00 | 4.74\* | .031 | .03 |
| *NR3C1* | cg27345592 | Chr5: 142786405 | 0.04 | .852 | .00 | 0.00 | .963 | .00 |
| *NR3C1* | cg06952416 | Chr5: 142781736 | 1.50 | .223 | .01 | 0.18 | .669 | .00 |
| *NR3C1* | cg06968181 | Chr5: 142784323 | 0.03 | .867 | .00 | 0.03 | .867 | .00 |
| *NR3C1* | cg27122725 | Chr5: 142781723 | 0.04 | .841 | .00 | 1.01 | .316 | .01 |
| *NR3C2* | cg02534661 | Chr4: 149364543 | 0.64 | .425 | .00 | 1.20 | .275 | .01 |
| *NR3C2* | cg05075176 | Chr4: 149362761 | 0.00 | .957 | .00 | 0.01 | .928 | .00 |
| *NR3C2* | cg05437692 | Chr4: 149362435 | 0.18 | .676 | .00 | 3.22 | .075 | .02 |
| *NR3C2* | cg07275757 | Chr4: 149189974 | 0.05 | .820 | .00 | 0.85 | .358 | .01 |
| *NR3C2* | cg07760722 | Chr4: 149033953 | 0.01 | .939 | .00 | 0.55 | .459 | .00 |
| *NR3C2* | cg10207656 | Chr4: 149019526 | 2.32 | .129 | .01 | 0.25 | .617 | .00 |

(continued)

**Table S6** (continued)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | ME EPDSpre | | | IA EPDSpre x sex | | |
| Gene | CpG | Position | *F* | *p* | ηp2 | *F* | *p* | ηp2 |
| *NR3C2* | cg10288772 | Chr4: 149363461 | 6.51\* | .012 | .04 | 1.01 | .318 | .01 |
| *NR3C2* | cg10590842 | Chr4: 149083955 | 2.02 | .157 | .01 | 3.38 | .068 | .02 |
| *NR3C2* | cg12841684 | Chr4: 149251768 | 0.30 | .586 | .00 | 0.19 | .663 | .00 |
| *NR3C2* | cg13000004 | Chr4: 149074093 | 0.09 | .759 | .00 | 0.13 | .722 | .00 |
| *NR3C2* | cg13996731 | Chr4: 149363522 | 1.38 | .242 | .01 | 0.86 | .356 | .01 |
| *NR3C2* | cg16692923 | Chr4: 149364700 | 0.89 | .347 | .01 | 0.19 | .667 | .00 |
| *NR3C2* | cg20140452 | Chr4: 149363715 | 2.30 | .085 | .02 | 0.83 | .364 | .01 |
| *NR3C2* | cg27460943 | Chr4: 149362809 | 2.27 | .134 | .01 | 0.00 | .971 | .00 |
| *NR3C2* | cg02471166 | Chr4: 149244985 | 0.36 | .551 | .00 | 0.15 | .703 | .00 |
| *SLC6A4* | cg01330016 | Chr17: 28549806 | 2.40 | .123 | .02 | 0.01 | .928 | .00 |
| *SLC6A4* | cg03363743 | Chr17: 28562474 | 0.00 | .973 | .00 | 0.07 | .795 | .00 |
| *SLC6A4* | cg05951817 | Chr17: 28562142 | 0.15 | .703 | .00 | 0.03 | .856 | .00 |
| *SLC6A4* | cg18584905 | Chr17: 28563300 | 5.19\* | .024 | .03 | 0.21 | .649 | .00 |
| *SLC6A4* | cg20592995 | Chr17: 28524160 | 3.41 | .067 | .02 | 0.01 | .939 | .00 |
| *SLC6A4* | cg22584138 | Chr17: 28562220 | 0.01 | .943 | .00 | 1.10 | .297 | .01 |
| *SLC6A4* | cg26126367 | Chr17: 28559497 | 2.11 | .148 | .01 | 0.29 | .594 | .00 |
| *SLC6A4* | cg26741280 | Chr17: 28563089 | 3.11 | .080 | .02 | 4.28\* | .040 | .03 |
| *SLC6A4* | cg06841846 | Chr17: 28564094 | 0.58 | .448 | .00 | 0.16 | .695 | .00 |
| *SLC6A4* | cg12074493 | Chr17: 28564117 | 0.68 | .411 | .00 | 0.46 | .497 | .00 |

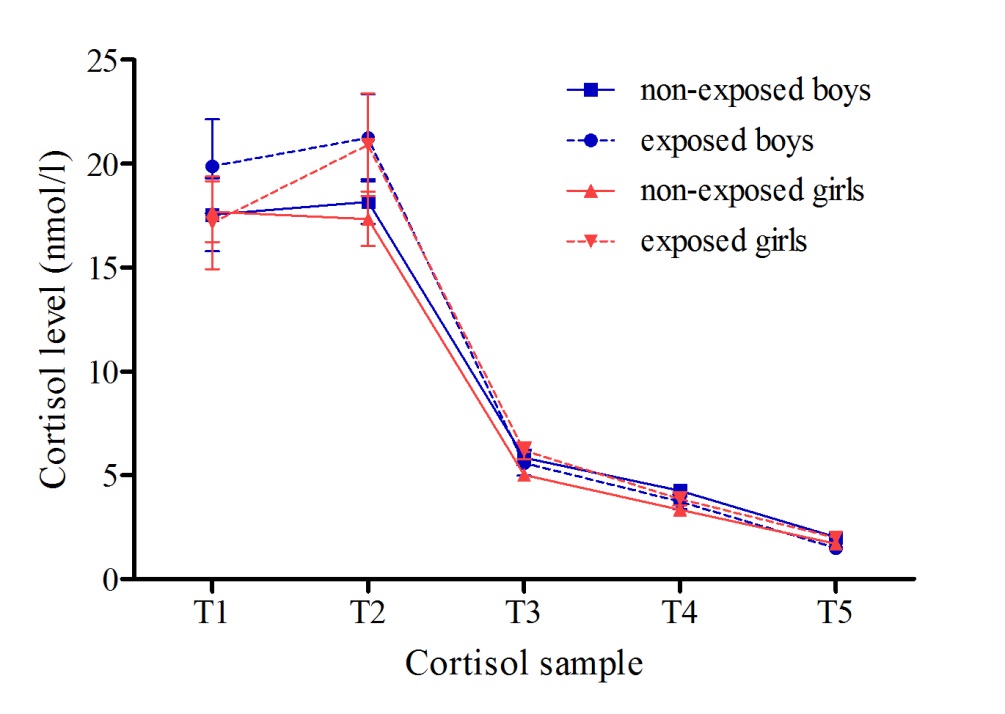
*Note*. *n* = 144-167 due to excluded methylation values of single CpGs. Maternal postnatal and current depressive symptoms were included as covariates. ME = main effect; IA = interaction effect. EPDS = Edinburgh Postnatal Depression Scale (Cox et al., 1987). EPDSpre = exposure to prenatal depressive symptoms (EPDS score ≥ 10) or no exposure (< 10). \**p* < .05. \*\**p* < .01

## Table S5. *DNA methylation as predictor of diurnal cortisol parameters: results of multiple regression models*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Diurnal cortisol slopea,b | | | | | | | | |
| Gene | CpG | All  (*n* = 99) | | | Boys  (*n* = 44) | | | Girls  (*n* = 55) | | |
| *β* | *t* | *p* | *β* | *t* | *p* | *β* | *t* | *p* |
| *NR3C1* | cg04111177 | -.08 | -0.80 | .426 | -.13 | -0.83 | .410 | -.03 | -0.24 | .815 |
| *NR3C1* | cg07733851 | -.10 | -0.97 | .332 | -.03 | -0.17 | .869 | -.12 | -0.92 | .364 |
| *NR3C1* | cg27107893 | -.07 | -0.62 | .536 | -.25 | -1.50 | .143 | .07 | 0.54 | .592 |
| *NR3C2* | cg10288772 | -.06 | -0.57 | .568 | .07 | 0.46 | .647 | -.16 | -1.27 | .211 |
| *SLC6A4* | cg18584905 | -.01 | -0.11 | .916 | .10 | 0.63 | .534 | -.11 | -0.84 | .407 |
| *SLC6A4* | cg26741280 | .06 | 0.60 | .551 | .07 | 0.46 | .647 | .04 | 0.32 | .754 |
|  |  | Bedtime Cortisola,b | | | | | | | | |
|  |  | All  (*n* = 144) | | | Boys  (*n* = 70) | | | Girls  (*n* = 74) | | |
| Gene | CpG | *β* | *t* | *p* | *β* | *t* | *p* | *β* | *t* | *p* |
| *NR3C1* | cg04111177 | -.06 | -0.77 | .446 | -.03 | -0.24 | .815 | -.09 | -0.80 | .425 |
| *NR3C1* | cg07733851 | -.01 | -0.13 | .900 | -.01 | -0.11 | .913 | .03 | 0.24 | .808 |
| *NR3C1* | cg27107893 | .00 | 0.02 | .981 | -.07 | -0.53 | .596 | .08 | 0.60 | .551 |
| *NR3C2* | cg10288772 | .09 | 1.13 | .262 | .30 | 2.64\* | .010 | -.07 | -0.65 | .519 |
| *SLC6A4* | cg18584905 | -.01 | -0.14 | .893 | -.01 | -0.07 | .944 | .02 | 0.19 | .852 |
| *SLC6A4* | cg26741280 | -.04 | -0.56 | .580 | -.11 | -0.99 | .327 | -.00 | -0.02 | .983 |
|  |  | Total cortisol releasea,c | | | | | | | | |
|  |  | All  (*n* = 144) | | | Boys  (*n* = 70) | | | Girls  (*n* = 74) | | |
| Gene | CpG | *β* | *t* | *p* | *β* | *t* | *p* | *β* | *t* | *p* |
| *NR3C1* | cg04111177 | .03 | 0.41 | .684 | .05 | 0.56 | .575 | -.00 | -0.00 | .995 |
| *NR3C1* | cg07733851 | -.12 | -1.83 | .069 | -.15 | -1.68 | .098 | -.07 | -0.81 | .419 |
| *NR3C1* | cg27107893 | -.02 | -0.28 | .778 | -.14 | -1.37 | .177 | .08 | 0.74 | .466 |
| *NR3C2* | cg10288772 | .03 | 0.48 | .630 | .03 | 0.30 | .768 | .03 | 0.29 | .773 |
| *SLC6A4* | cg18584905 | -.03 | -0.48 | .630 | -.06 | -0.59 | .556 | -.01 | -0.14 | .890 |
| *SLC6A4* | cg26741280 | .01 | 0.15 | .883 | .04 | 0.47 | .638 | -.01 | -0.09 | .926 |

*Note*. Specific covariates for the cortisol parameters were included in the models: atime between first and last sample. bmean Apgar score. cschool day (yes/no). \**p* < .05

## Figure S1.



***Figure S1****.* Child diurnal cortisol profiles, separately for children non-exposed vs. exposed to prenatal depressive symptoms and sex (*n* = 98-146). Default sampling times: T1 = at awakening, T2 = 30 minutes after awakening, T3 = 12 a.m., T4 = 5 p.m., T5 at bedtime. Prenatal EPDS (Edinburgh Postnatal Depression Scale; Cox et al., 1987) score <10 interpreted as non-exposed, ≥10 as exposed.

## Figure S2

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| PCs of Control Probe PCA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|  | PC1 | | PC2 | | PC3 | | PC4 | | PC5 | | PC6 | | PC7 | | PC8 | | PC9 | | PC10 | | PC11 | | PC12 | | PC13 | | PC14 | | PC15 | |  | | | |  | | |  | |
| Plate |  | |  | | 0.42 | |  | |  | | 0.14 | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | | | |  | | |  | |
| Chip |  | | 0.13 | | 0.91 | | 0.81 | | 0.45 | | 0.43 | | 0.13 | |  | | 0.23 | | 0.61 | |  | | 0.13 | | 0.10 | | 0.17 | | 0.22 | |  | | | |  | | |  | |
|  | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|  | PC16 | | PC17 | | PC18 | | PC19 | | PC20 | | PC21 | | PC22 | | PC23 | | PC24 | | PC25 | | PC26 | | PC27 | | PC28 | | PC29 | | PC30 | |  | | | | *R*2 = 1.00 | | | | |
| Plate |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | | | |  | | |  | |
| Chip | 0.14 | | 0.21 | | 0.11 | |  | | 0.10 | |  | |  | |  | |  | |  | |  | |  | | 0.14 | |  | |  | |  | | | |  | | |  | |
|  |  |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | | | |  | | |  |
|  |  |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | | | |  | | |  |
| PCs of PCA after correction for 23 Control Probe PCs | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|  | PC1 | | PC2 | | PC3 | | PC4 | | PC5 | | PC6 | | PC7 | | PC8 | | PC9 | | PC10 | | PC11 | | PC12 | | PC13 | | PC14 | | PC15 | |  | | |  | | |  | | |
| Plate |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | | | |  | | |
| Chip |  | | 0.10 | |  | | 0.13 | | 0.11 | | 0.18 | | 0.14 | | 0.10 | | 0.15 | |  | |  | | 0.19 | |  | |  | | 0.14 | |  | | *R*2 = 0.00 | | | | | | |
|  | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|  | PC16 | | PC17 | | PC18 | | PC19 | | PC20 | | PC21 | | PC22 | | PC23 | | PC24 | | PC25 | | PC26 | | PC27 | | PC28 | | PC29 | | PC30 | |  | |  | | | |  | | |
| Plate |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | |  | | | |  | | |
| Chip | 0.10 | |  | | 0.10 | |  | |  | |  | | 0.10 | |  | | 0.10 | |  | |  | | 0.12 | |  | |  | |  | |  | |  | | | |  | | |

***Figure S2.***Results of the principle component analyses (PCAs) within the Control Probe Adjustment (Lehne et al., 2015), indicating technical biases due to plate and chip. *R2* values represent plate and chip effects before and after correction for 23 control probe principal components (PCs). Only *R2* values ≥ .10 are indicated.

## Figure S3.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| SES |  |  |  |  |  |  |  |  |  |  |  |  |
| Age |  |  |  |  |  |  |  |  |  |  |  | *p* = .000 |
| Sex |  |  |  |  |  |  |  |  |  |  |  |  |
| SDQ emotional |  |  |  |  |  |  |  |  |  |  |  |  |
| SDQ conduct | -.141 |  |  |  |  |  |  |  |  |  |  |  |
| Gestational age |  |  |  |  |  |  |  |  |  |  |  |  |
| Birth weight |  |  |  |  |  |  |  |  |  |  |  |  |
| Maternal age at birth |  |  |  |  |  |  |  |  |  |  |  |  |
| Apgar |  |  |  |  |  |  |  |  |  |  |  |  |
| Alcohol consumption pre |  |  |  |  |  |  |  | .255\*\* |  |  |  |  |
| Cigarette smoking pre |  |  |  | .149 |  |  |  |  | .163\* |  |  |  |
| EPDS pre |  |  | -.185\* |  |  |  |  |  |  |  |  |  |
| EPDS post |  |  |  |  |  |  |  |  |  |  |  |  |
| EPDS current |  |  |  | -.170\* | -.134 |  |  |  |  |  |  | *p* = .100 |
|  | PC1 | PC2 | PC3 | PC4 | PC5 | PC6 | PC7 | PC8 | PC9 | PC10 |  |  |

***Figure S3.***Associations of PCs and relevant psychosocial variables after adjustment for 23 control probe factors. sex and birth parameters within the Control Probe Adjustment (Lehne et al., 2015). Correlations are Pearson product-moment-correlation coefficients. Only coefficients with a *p*-value ≤ .10 are displayed. PC1 and PC2 were included as predictors in a final regression model to account for further biological variance. SES = socioeconomic family status. SDQ = Strength and Difficulties Questionnaire (Goodman, 2001), emotional = SDQ subscale ‘Emotional Problems’, conduct = SDQ subscale ‘Conduct Problems’. EPDS = Edinburgh Postnatal Depression Scale (Cox et al., 1987). Pre = prenatal, post = postnatal. \**p* < .05, \*\**p* < .01

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